Complete Summary

GUIDELINE TITLE

Hypopharyngeal cancer.

BIBLIOGRAPHIC SOURCE(S)

Dutch Head and Neck Oncology Cooperative Group. Hypopharyngeal cancer. Amsterdam, The Netherlands: Association of Comprehensive Cancer Centres; 2007 Jan 9. 209 p. [904 references]

GUIDELINE STATUS

This is the current release of the guideline.

The guideline will be updated annually by a multidisciplinary committee created in 2006 based on scientific developments. The Dutch Head and Neck Oncology Cooperative Group, as the primary party responsible for the current guideline, will furnish the chairperson for this multidisciplinary committee. The committee has the responsibility of making interim inquiries by professional societies to establish the need for revision(s) of the current guideline. For important developments, it can be decided in agreement with CBO and VIKC to create interim electronic amendments and distribute them through the various professional societies. If necessary, a new study group will be created to revise the guideline or parts of it. The committee will install a new multidisciplinary study group for a complete revision of the guideline by no later than 2011.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Primary, metastatic, and recurrent hypopharyngeal cancer

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Dentistry
Family Practice
Internal Medicine
Nuclear Medicine
Nursing
Nutrition
Oncology
Otolaryngology
Pathology
Physical Medicine and Rehabilitation
Plastic Surgery
Psychiatry
Psychology
Radiation Oncology
Radiology
Speech-Language Pathology
Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Dentists
Dietitians
Health Care Providers
Nurses
Physical Therapists
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers
Utilization Management

GUIDELINE OBJECTIVE(S)

- To achieve uniformity among treatment centres with regard to the diagnosis and treatment of hypopharyngeal cancer
- To define the framework within which multidisciplinary care should occur
- To discuss specific indications for organ-sparing therapy and the optimal approach to organ-sparing therapy

TARGET POPULATION

People in the Netherlands with hypopharyngeal cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Medical history
    - Signs and symptoms
    - Tobacco and alcohol use
    - Occupational risks
2. Clinical examination
3. Endoscopy
4. Diagnostic imaging: computed tomography (CT) scan and magnetic resonance imaging (MRI)
5. Tumor volume assessment
    - Metastases
    - Second primary tumor
6. Panendoscopy
7. Bronchoscopy
8. Oesophagoscopy
9. Thoracic x-ray
10. Fluorodeoxyglucose positron emission tomography (FDG-PET) scan
11. Patient and family counseling
12. Bilateral staging of cervical lymph node metastases
    - CT or MRI
    - Ultrasound with fine needle aspiration
13. Chest CT as indicated to diagnose distant metastases
14. Tumor-node-metastasis (TNM) staging
15. Functional scoring (Karnofsky, World Health Organization [WHO])

Management/Treatment

1. Radiotherapy
    - Conventional fractionation
    - Accelerated fractionation
    - Hyperfractionation
    - Concomitant radiotherapy boost
    - Sites of irradiation
2. Chemoradiation
3. Surgery with postoperative radiotherapy or chemoradiation
    - Cervical lymph node dissection
    - Total laryngectomy with total or partial pharyngectomy
4. Management of complications
5. Counseling and communication (patient and family involvement in decisions, treatment risk assessment)
6. Follow-up
    - Schedule of visits
    - Thyroid function
7. Supportive care
    - Swallowing rehabilitation

- Speech therapy
- Smoking and alcohol cessation
- Oral hygiene, dental care
- Nutrition and dietary therapy

8. Palliative care
    - Palliative chemotherapy
    - Palliative radiotherapy
    - Palliative surgery
    - Pain management

MAJOR OUTCOMES CONSIDERED

- Mortality
- Complications and side effects of radiotherapy, chemoradiation, and surgery
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The recommendations in this guideline are based as much as possible on evidence from published scientific research. Relevant articles were found by performing systematic searches in the Cochrane Library, Medline, Embase, Cinahl, and Psychinfo. Searches were limited to articles published in English, German, French, and Dutch. Manual searches were also performed, and articles were extracted from the reference lists of the articles retrieved. Other recent guidelines on head and neck cancer were also consulted. The search period was 1995-2005; some more recent articles were also included. Search terms for the patient population were hypopharyngeal neoplasms and head and neck neoplasms, used as free-text search and Medical Subject Headings (MESH); hypopharyngeal carcinoma, hypopharyngeal cancer, hypopharyngeal malignancy, and hypopharyngeal tumour were used as free-text search only. The following MESH terms were also used: gingival neoplasms, palatal neoplasms, tongue neoplasms, laryngeal neoplasms, pharyngeal neoplasms, and squamous cell carcinoma. Articles were selected based on the following criteria: comparative studies with a high level of evidence, such as meta-analyses, systematic reviews, randomised controlled trials (RCTs), and controlled trials (CT). When these studies were not available, further searches were performed for comparative cohort studies, comparative patient-control studies, and non-comparative studies. Other important criteria were sufficient follow-up, sufficient exclusion of selection bias, and applicability to the situation in the Netherlands.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Classification of Supporting Evidence Based on the Level of Evidence and Cervical Lymph Node Levels*

For Articles Regarding Intervention

A1	Systematic reviews covering at least some A2-level studies in which the results of the individual studies are consistent
A2	Randomised comparative clinical studies of good quality and sufficient size and consistency
B	Randomised clinical trials of moderate quality or insufficient size, or other comparative studies (non-randomised, comparative cohort studies, patient-control studies)
C	Non-comparative studies
D	Expert opinion from, for example, working group members

For Article Regarding Diagnosis

A1	Studies on the effects of diagnosis on clinical outcomes in a prospectively followed, well defined patient population with a predefined protocol based on the results of the study test, or decision theory studies on the effects of diagnosis on clinical outcomes based on the results of A2-level studies with sufficient consideration given to the interaction between diagnostic tests
A2	Studies that include a reference test with predefined criteria for the study test and the reference test and a good description of the test and the clinical population studied; a sufficiently large series of consecutive patients must be included, predefined cut-off values must be used and the results of the test and the gold standard must be evaluated independently. For situations in which multiple diagnostic tests are involved, there is in principle interaction and the analysis should take this into account by using, for example, logistical regression
B	Comparison with a reference test and description of the study test and population, but lacking the other characteristics of A-level studies
C	Non-comparative studies
D	Expert opinion from, for example, working group members

*See the original guideline document for a classification of cervical lymph node levels.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The quality of these articles was judged by working group members using the evidence-based guideline evaluation form. Articles of mediocre or poor quality were excluded. After this selection process, the remaining articles were then used as the basis for the various conclusions stated in the guideline. The selected articles were then graded according to the level of evidence using the classification. The level of evidence is reported in the conclusion section of each chapter. Key articles upon which the conclusion was made are also listed.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guideline 'Hypopharyngeal cancer' was developed through the Evidence-Based Guideline Development (Evidence-Based Richtlijn Ontwikkeling, EBRO) programme of the Dutch Society of Medical Specialists (Orde van Medisch Specialisten).

Composition of the Working Group

To create the guideline, a multidisciplinary working group was formed in 2004 that consisted of representatives from all specialties relevant to the diagnosis and treatment of hypopharyngeal cancer, including medical and paramedical specialists, epidemiologists, representatives from patient organisations, and colleagues from the Dutch Association of Comprehensive Cancer Centres (Vereniging van Integrale Kanker Centra, [VIKC] and the Dutch Institute for Healthcare Improvement (Kwaliteitsinstituut voor de Gezondheidszorg [CBO], see Appendix 3 in the original guideline document). Consideration was given to the geographic distribution of working group members and the balance of different organisations, institutions, and academic backgrounds. Working group members acted independently and with the approval of their associations.

Description of Problem and Basis Questions

The multidisciplinary committee that composed this guideline formulated a number of basis questions (see Appendix 11 in the original guideline document) that encompass policy issues in the diagnosis, treatment, and counselling of patients with hypopharyngeal cancer. These questions address the incidence, pathogenesis, and symptomatology of hypopharyngeal cancer, and factors that

influence the disease course, diagnosis, and treatment options, including their efficacy and impact on quality of life. Some chapters also describe appropriate measures for the psychosocial management of patients with hypopharyngeal cancer. The basis questions form the foundation of each chapter of the guideline. The guideline is therefore not intended to be comprehensive. Some additional instructional chapters have also been included.

Methods of the Working Group

Given the scope of the project, the guideline was divided into chapters during the first plenary meeting, authors and co-authors were assigned to each chapter, and the data to be used in the first draft of each chapter were confirmed. The editorial team, consisting of the chairs, the CBO advisor, and the VIKC project manager, were responsible for coordination and uniformity. Working group members worked on the text for the draft guidelines for approximately 1.5 years. Working group members wrote portions of text independently or in groups; the text was discussed during plenary meetings and, after comments were incorporated, harmonised. After harmonisation, the definitive draft guideline was published online (www.nwhht.nl) so that commentary from the community could be gathered at an early stage of the process and incorporated as necessary. The complete working group met 11 times to discuss the results of subgroups and the intercorrelation of results. The editorial team collected the texts developed by the subgroups and made any necessary changes for consistency to ultimately create one document: the draft guideline.

Development of the Recommendations

In addition to the scientific evidence, there are often other important aspects to consider in the development of a recommendation, including patient preference, the availability of special techniques or expertise, organisational factors, social consequences, and costs. These factors are addressed in the section following the 'Conclusions' in the original guideline document. In this section, the conclusion that was based on the literature is placed in the context of daily practice and the advantages and disadvantages of the various protocol options are weighed. The final formulated recommendation is the result of the available evidence in combination with these considerations. The output of this procedure and the structuring of the guideline in this format are intended to enhance the transparency of the guideline. It allows efficient discussion during the study group meetings and also increases the clarity for guideline users. This was presented for commentary at the national guideline conference on 26 September 2006.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Level of Evidence for Conclusions	
1	At least one systematic review (A1) or two independently conducted A2-level studies
2	At least two independently conducted B-level studies
3	At least one A2-, B- or C-level study

Level of Evidence for Conclusions	
4	Expert opinion from, for example, working group members

COST ANALYSIS

Published cost analyses were reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After comments from the national guideline conference on 26 September 2006 were incorporated, the guideline was confirmed by the entire working group on 9 January 2007 and sent for approval to the relevant professional societies. (see Appendix 2 in the original guideline document).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Epidemiology

Hypopharyngeal cancer is uncommon in the Netherlands, but there is a trend toward an increase in incidence. Hypopharyngeal cancers are more common in men than women. Most patients are diagnosed with advanced-stage disease. The 5-year survival rate is approximately 35% but depends on the stage of disease.

Aetiology

The use of tobacco and alcohol alone or in combination are the most important risk factors for developing hypopharyngeal cancer. Discouraging tobacco and alcohol use is an important component of primary and secondary prevention.

Smoking cessation reduces the risk of developing hypopharyngeal cancer gradually.

Workers in certain industries have an increased risk of developing hypopharyngeal cancer.

Diagnosis

Early Diagnosis

As part of general health advice, all tobacco use and excessive alcohol consumption should be discouraged immediately. Hypopharyngeal cancer should

be considered for patients who present with signs and symptoms of dysphagia, sore throat, pain radiating to the ear, hoarseness, swollen cervical lymph nodes, and/or stridor. If hypopharyngeal cancer is considered, information on tobacco and alcohol use should be collected as part of the patient history. The patient should be referred to an otorhinolaryngologist if symptoms persist for more than three weeks.

Diagnosis of Primary Tumour

Clinical examination and endoscopy are indicated for the diagnosis of hypopharyngeal cancer, particularly to determine the extent of disease and to assess laryngeal mobility.

Imaging with computed tomography (CT) or magnetic resonance imaging (MRI) is advised to determine the extent of disease in deep-lying and adjacent structures.

For the diagnosis of hypopharyngeal cancer, a combination of clinical examination, endoscopy, and CT/MRI is recommended.

Diagnostic Imaging

The working group is of the opinion that CT and MRI have an indispensable role in the diagnosis and staging of hypopharyngeal cancer.

The technique and performance of both CT and MRI assessment must meet strict minimum requirements.

The risk of producing motion artefacts should be reduced as much as possible.

Volume Assessment

The working group is of the opinion that:

- CT and MRI are reliable methods for assessing tumour volume for hypopharyngeal cancer.
- Assessment should be performed by an expert in the field of head and neck radiology whenever possible to reduce variability.
- Reporting of imaging results should meet strict minimal requirements.

Cartilage Invasion

CT and MRI are the preferred modalities for determining cartilage infiltration by an invasive hypopharyngeal cancer. To prove cartilage involvement using CT, a number of criteria must be demonstrated (sclerosis, erosion, lysis, infiltration of soft tissue). The risk of cartilage invasion increases as the number of criteria present increases.

If MRI is used, one should be aware of the potential risk of overestimating the extent of disease.

Prevertebral Invasion

Perioperative palpation is recommended to determine whether hypopharyngeal cancer has invaded the prevertebral space.

Imaging with CT or MRI has a modest role in the preoperative evaluation of this area.

Diagnosis of Multiple Primary Tumours

Given the high incidence of multiple primary tumours in patients with hypopharyngeal cancer and their potential consequences, the working group considers a thorough patient history and physical examination essential. The patient history and physical examination should be directed not only toward local problems but also toward the possible presence of multiple primary tumours.

There is no consensus in the literature regarding the appropriateness of supplemental tests. Endoscopic assessment of the oral cavity, pharyngeal axis, and larynx is an essential component of diagnosis. The working group recommends radiological analysis only if justified based on the symptoms present. Bronchoscopy and evaluation of the oesophagus should be performed if indicated. Regarding oesophageal assessment, oesophagoscopy is preferred over x-ray.

A fluorodeoxyglucose positron emission tomography (FDG-PET) scan can provide additional information, but insufficient data are available to recommend it as part of the standard diagnostic work-up at this time.

Counselling and Communication

Structurally standardised counselling should be offered to patients with head and neck cancer and their family members.

Counselling patients with head and neck cancer should cover not only the biomedical aspects of diagnosis and treatment but also how the treatment process works, the prognosis and life expectancy, and the expected short-term and long-term effects on daily living.

Nurses should play a prominent role in counselling patients on treatment and the expected disability due to the disease or treatment. Other professionals involved in patient care also play a role in counselling.

Written information should accompany verbal counselling. Audio cassettes and other modern audiovisual devices can enhance the provision of information. These approaches may be used to supplement - but not replace - verbal counselling.

Patients are not expected to hear and retain all of the information provided during counselling. Therefore, it should be checked at a later time whether the patient in fact received and understood the necessary information.

Counselling is most effective when it is tailored to the individual needs of the patient. Standardised quality of life questionnaires are helpful in screening for the presence of somatic and psychosocial issues, and are therefore recommended.

Treatment

Organ-sparing approaches (larynx/pharynx) are preferred in the management of hypopharyngeal cancer. If non-surgical, organ-sparing therapy is desired, the preferred approach is primary radiotherapy for small tumours and concomitant chemoradiation for more advanced stages of disease. See also the sections on "Decision-Making" and "Counselling and Communication," below.

T1-2N0

Treatment of T1N0 and T2N0 hypopharyngeal cancers consists of primary radiotherapy of the primary tumour and elective bilateral radiotherapy of the neck (levels II-IV; level VI and retropharyngeal nodes as indicated). The dose for elective radiotherapy of lymph nodes is 46 Gy in 2-Gy fractions or equivalent. For T1 tumours, a conventional radiotherapy fractionation schedule is used. For T2 or greater tumours, accelerated or hyperfractionated schedules are preferred. Example schedules include that used in the Danish Head and Neck Cancer Study (DAHANCA) trial (68-70 Gy in 2-Gy fractions, 6 fractions/week for 38-40 days), the European Organisation for Research and Treatment of Cancer (EORTC) trial (80.5 Gy in 1.15-Gy fractions, 2 fractions/day for 47 days), or the concomitant boost technique used in the Radiation Therapy Oncology Group (RTOG) trial (72 Gy in 1.8-Gy fractions plus a 1.5-Gy booster as second daily fraction for the last 12 days of a 40-day treatment period).

See also the "Summary" section below.

T3-4N0

Non-surgical organ-sparing therapy, such as concomitant chemoradiation, is preferred for T3N0 and T4N0 tumours. If chemoradiation is not possible, primary radiotherapy using an alternative fractionation schedule (see above) is recommended. If the probability of preserving laryngeal and/or pharyngeal function after chemoradiation is low, the treatment of choice is surgery with postoperative radiotherapy or chemoradiation.

See also the "Summary" section below.

T1-4N+

T1-2N2a, N2b, Extensive N2c More Than 3 cm, or N3

If the primary tumour is small (T1 or T2) with N2a of N3 disease of the neck, the preferred approach is cervical lymph node dissection followed by primary radiotherapy of the tumour.

With regard to postoperative radiotherapy or chemoradiation for N0 or N+ disease, see the relevant sections on postoperative radiotherapy, below.

Stage T1-2N2b-2c hypopharyngeal cancer can be treated with primary radiotherapy and cervical lymph node dissection of residual nodes. Conventionally fractionated radiotherapy is recommended for T1 tumours, and alternatively

fractionated radiotherapy is recommended for T2 tumours. For cases of extensive N2b or N2c disease, particularly those with lymph node clumping, the preferred treatment is similar to that for N2a or N3 disease: cervical lymph node dissection followed by primary radiotherapy of the tumour.

See also the "Summary" section below.

T3-4N1-3 and Unresectable Tumours

Chemoradiation is the treatment of choice for patients with hypopharyngeal cancer and unresectable tumours and/or lymph nodes who are aged 18-60 years and have a Karnofsky score of at least 80% or World Health Organization (WHO) functional class 0-1. Chemoradiation may be considered for patients aged 60-70 years with a good Karnofsky score. Non-surgical organ-sparing therapy is preferred for T3-4N+ hypopharyngeal cancer due to its comparable chance of cure and a good chance of preservation of laryngeal and/or pharyngeal function. Chemoradiation is preferred for patients with T3-4 tumours aged less than 60 years and a Karnofsky score of at least 80% or WHO 0-1. Chemoradiation may be considered for patients aged 60-70 years. Chemotherapy should be given concomitantly with radiotherapy (e.g., cisplatin 100 mg/m^2 in weeks 1, 4, and 7 with conventionally fractionated radiotherapy) preferably 70 Gy in 35 fractions, 5 fractions/week for 47 days. An alternative to chemoradiation is alternative fractionation. Examples include the schedule used in the DAHANCA trial (68-70 Gy in 2-Gy fractions, 6 fractions/week for 40 days), the EORTC trial (80.5 Gy in 1.15-Gy fractions, 2 fractions daily for 47 days), or the concomitant boost technique used in the RTOG trial (72 Gy in 1.8-Gy fractions with a 1.5-Gy booster as second daily fraction during the last 12 days). The interfraction interval for hyperfractionation (HF) should be at least 6 hours, preferably 8 hours.

Patients with complete remission of the primary tumour but persistent or progressive lymph nodes 6-8 weeks after radiotherapy or chemoradiation should undergo (selective) cervical lymph node dissection. Planned cervical lymph node dissection should be strongly considered for patients with initial N3 disease who achieve clinical and radiological complete remission in the neck and complete remission in the primary tumour after radiotherapy or chemoradiation. If cervical lymph node dissection is performed, selective cervical lymph node dissection is preferred.

For patients with T4 tumours and extensive involvement of cartilage and/or soft tissue, the preferred approach is total laryngectomy with total or partial pharyngectomy and ipsilateral cervical lymph node dissection for N+ disease, followed by postoperative radiotherapy or chemoradiation (see "Postoperative Radiotherapy," below).

See also the "Summary" section below.

Postoperative Radiotherapy

Postoperative radiotherapy is indicated for patients with squamous cell carcinoma of the head and neck and micro- or macroscopic non-radical resection <1 mm, two or more lymph node metastases, and/or extranodal growth of one lymph node greater than 3 cm (primary criteria). Postoperative radiotherapy is advisable

for patients with T3 or T4 disease, narrow resection margins (1-5 mm), perineural growth, and an infiltrative pattern of growth (secondary criteria). Based on the presence of primary and secondary criteria, patients can be classified into the following risk groups:

- Intermediate risk: T3 or T4 disease, perineural growth, an infiltrative pattern of growth, 2 or more lymph node metastases, lymph node metastases >3 cm, BUT resection margins of 5 mm or more, no extranodal growth, and no N3 disease
- High risk: T1, T2, or T4 disease with a resection margin less than 5 mm, one lymph node metastasis with extranodal growth
- Very high risk: T3 disease with a resection margin less than 5 mm, two or more lymph node metastases with extranodal growth, N3 disease

The dose of postoperative radiotherapy for hypopharyngeal cancer is at least 56 Gy for the intermediate risk group and 66 Gy for the high and very high risk groups, according to the new recursive partitioning analysis (RPA) classification (i.e., RPA class 2 and 3). The dose for elective radiation of lymph node stations is 46 Gy.

Postoperative chemoradiation for hypopharyngeal cancer is recommended for patients younger than 60 years with a good Karnofsky score, extranodal growth in one or more lymph node metastases, and/or non-radical resection (<1 mm). Postoperative chemoradiation can be strongly considered for patients with N3 disease. Postoperative chemoradiation can also be considered for patients aged 60-70 years who meet the aforementioned criteria and are in excellent physical condition.

Postoperative chemoradiation for hypopharyngeal cancer consists of platinum-based chemotherapy (preferably cisplatin) and a conventional fractionation schedule up to a dose of 66 Gy.

For patients with hypopharyngeal cancer who do not meet the criteria for postoperative chemoradiation, and for those who are ineligible for chemoradiation due to medical reasons, postoperative radiotherapy can be given using a conventional fractionation schedule. Postoperative alternative fractionation does not yet have a role outside the context of a clinical trial.

The goal is to achieve the shortest possible interval between surgery and the start of radiotherapy or chemoradiation, preferably within six weeks.

Selection of lymph node levels to be irradiated postoperatively is similar to that for primary radiotherapy for patients with hypopharyngeal cancer and N0 or N+ disease.

See also the "Summary" section below

Complications

Chyle Leakage After Cervical Lymph Node Dissection

Patients who develop chyle leakage after cervical lymph node dissection should be started immediately on a low-long-chain triglyceride (LCT), high-medium-chain triglyceride (MCT) oral diet. If the chyle leakage does not respond sufficiently, the patient may be switched to low-fat tube feeding or total parenteral feeding (TPF). Re-exploration of the neck is indicated if there is still insufficient effect.

To prevent deterioration of nutritional status, feeding should be enriched with carbohydrates and/or protein.

Hypothyroidism

Given the high incidence of hypothyroidism after treatment for hypopharyngeal cancer, thyroid function should be monitored, preferably every 6 months in the first 5 years and annually thereafter. If the thyroid stimulating hormone (TSH) increases, the patient should be referred to an internist/endocrinologist.

*Toxicity and Complications of Radiotherapy and Chemoradiatio*n

Radiation damage and particularly late effects should be graded and recorded as carefully and completely as possible. Grading is preferably done according to the NCI Common Toxicity Criteria (CTC), but at least according to the recommendations regarding the recording of complications developed by the Dutch Society of Radiotherapy and Oncology (NVRO).

To prevent late radiation effects when using accelerated fractionation, it is essential to maintain a sufficiently long interfraction interval (at least 6 hours, preferably 8 hours).

To prevent osteoradionecrosis, dental surgery should be performed prior to starting radiotherapy (see "Oral Hygiene", below).

Hyperbaric oxygen therapy can be considered for the treatment of severe laryngeal chondronecrosis and mandibular osteoradionecrosis.

Decision-Making

After sufficient counselling, patients with hypopharyngeal cancer and their family members should be involved in making treatment decisions. In the care provider-patient dialogue, all facets of the available treatment options should be explored, including the outcomes and side effects expected for that patient. The working group is of the opinion that a treatment plan drafted by a multidisciplinary team should be presented to the patient with hypopharyngeal cancer. If there are multiple treatment options, the multidisciplinary team should provide a recommendation. To accomplish this, the care provider must be aware of the patient's fears, perceptions, and priorities.

Counselling and Communication

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Summary

Summary of recommendations for the treatment of hypopharyngeal cancer:

Location	T-N Stage	Treatment of Choice
Posterior hypopharyngeal wall	T1-2N0,N+ <3 cm	Primary radiation therapy (RT) to tumour and bilateral neck; elective to levels II-IV and retropharyngeal lymph nodes (conventional for T1; accelerated fractionation or hyperfractionation for T2)
Lateral and medial wall of the piriform sinus	T1-2N0,N+ <3 cm	Primary RT to the bilateral neck; elective levels II-IV and level VI (conventional for T1; accelerated fractionation or hyperfractionation for T2)
Other sites	T1-2N0,N+ <3 cm	RT to tumour and bilateral cervical lymph nodes; elective levels II-IV, retropharyngeal lymph nodes for postcricoid cancer, level VI for postcricoid cancer or apical piriform sinus (conventional for T1; accelerated fractionation or hyperfractionation for T2)
All sites	T1-2N2 bulky, N3	Cervical lymph node dissection prior to RT; RT of primary tumour and bilateral neck. Postoperative chemoradiation for extranodal growth and/or non-radical resection (aged < 60(70) years and World Health Organization [WHO] 0-1). Strongly consider postoperative

Location	T-N Stage	Treatment of Choice
		chemoradiation for N3 disease. For other cases: conventional fractionation for T1 and alternative fractionation for T2
All sites	T3-4 any N	Chemoradiation for patients aged ≤60(70) years and WHO 0-1. Accelerated RT or hyperfractionation for patients aged >(60)70 years. Cervical lymph node dissection 6-8 weeks after RT for all cases of persistent or progressive residual lymph nodes, and strongly considered for initial N3 disease
All sites	T4 afunctional larynx	Surgery plus postoperative radiotherapy or chemoradiation
All sites	Unresectable T and/or N	Chemoradiation for patients aged ≤60(70) years and WHO 0-1; accelerated RT or hyperfractionation for patients aged >(60)70 years. Cervical lymph node dissection after RT as indicated if complete response of primary tumour
All sites	(Palliation)	Palliative RT, methotrexate, or watchful waiting

Follow-Up

Schedule of follow-up visits

	Year 1	Year 2	Year 3	Year 4	Year 5
Interval, months	2-3	3	4-6	6	6

This schedule should be followed until new data become available.

Annual or semi-annual chest x-ray does not appear to be beneficial.

Hypothyroidism

For all patients in whom the thyroid lay partially or entirely within the radiation field, it is advisable to check thyroid function **routinely** (e.g., every 6 months) throughout the entire follow-up period.

Local Recurrence: Diagnosis and Treatment

In patients suspected of having recurrent/residual hypopharyngeal cancer, pharyngoscopy and biopsy should be performed only if clinical symptoms are present.

In patients suspected of having regional recurrence, fine needle aspiration should be performed only if clinical symptoms are present.

In patients suspected of having residual hypopharyngeal cancer, FDG-PET should be performed no sooner than three months after chemoradiation.

In cases where it is difficult to differentiate between radiation effects and recurrent/residual hypopharyngeal cancer, FDG-PET may be useful and obviate the need for pharyngoscopy. If the FDG-PET is negative, a watchful-waiting approach is reasonable.

Additional surgery can be withheld if the FDG-PET following radical radiotherapy is negative in a patient who initially had lymph node metastases <3 cm.

Metastases: Diagnosis

Cervical Lymph Node Metastases

Bilateral staging of the neck using imaging techniques is indicated for all patients with hypopharyngeal cancer.

For levels I-VI, ultrasound with fine needle aspiration is preferred.

The working group advises that ultrasound with fine needle aspiration is preferably performed in a treatment centre, ideally by a radiologist with the relevant expertise.

CT and/or MRI are necessary to image retropharyngeal lymph nodes.

The working group recommends fine needle aspiration cytology for all lymph nodes with a short-axial diameter of 5 mm or more. If a selective approach is used due to the high number of affected lymph nodes, at least the lymph nodes from the first nodal station should be aspirated.

Distant Metastases

Screening for distant metastases using chest CT is indicated for patients with hypopharyngeal cancer, provided that they have:

- Three or more lymph node metastases
- N2c or N3 disease
- Low jugular lymph node metastases
- A second primary tumour

Supportive Care

Support and Rehabilitation

The working group is of the opinion that:

- A speech therapist should be included in the support and rehabilitation team for patients with hypopharyngeal cancer
- The speech therapist can be called in prior to treatment for patient counselling and advice, if severe swallowing and/or speech impairment is expected as a result of radiotherapy or chemoradiation
- Check-ups that give special attention to swallowing and speech issues should be incorporated into the follow-up plan
- Swallowing and speech rehabilitation following oncological treatment should be initiated in a logopaedic centre that has expertise in this area and is preferably associated with the treatment centre where primary treatment occurs

Fatigue

Intervention for fatigue must focus on identifying the physical cause and helping the patient to recognise the pattern of fatigue.

In addition to verbal and written information on fatigue, the national rehabilitation programmes "Herstel en Balans" and "Verder in Balans" can be offered to patients.

Volunteer Care

Volunteer care plays an important role in patient quality of life. Volunteer care should be incorporated into the clinical and outpatient phases of care.

Smoking and Alcohol

It is important to actively follow anti-smoking and alcohol policies.

All patients with hypopharyngeal cancer who smoke should receive advice on how to stop smoking. Help with smoking cessation can be provided in the form of discussions, nicotine substitution, pharmacological support, and informational brochures.

Further information can be found in the evidence-based guideline (in Dutch) Tobacco addiction.

To prevent alcohol withdrawal symptoms, it is advisable to follow a protocol that describes the various interventions, such as the provision of medication and informational brochures, and referral to general practitioners and care-providing organisations.

If a patient develops delirium, refer to the evidence-based guideline (in Dutch) Delirium.

Physiotherapy

Lower trapezius muscle function should be evaluated in patients who have undergone cervical lymph node dissection.

Physiotherapy is recommended for patients with dysfunction of the lower trapezius muscle.

Oral Hygiene

The working group is of the opinion that:

- Prior to receiving oncology care, patients with hypopharyngeal cancer should be seen by a dental surgery team, consisting of an maxillofacial surgeon, oral hygienist, and dentist, to identify and treat foci.
- Patients should rinse the mouth frequently during radiotherapy using a salt/soda solution.
- To prevent radiation-induced dental decay, dentate patients undergoing radiotherapy in the head and neck region should apply a 1% neutral NaF gel to the teeth daily, preferably using fluoride caps, in addition to following an proper oral hygiene regimen.
- There is insufficient evidence to justify the use of PTA lozenges or paste (polymyxin 2 mg, tobramycin 1.8 mg, amphotericin B 10 mg) to help prevent radiation-induced mucositis.
- A protective cap (e.g., fluoride cap) can be worn during radiotherapy to prevent radiation-induced tissue damage in the form of mucositis.

Nutrition and Dietary Therapy

The working group is of the opinion that, given the complex nutritional issues present, a specialised dietician should be included in the treatment team for patients with hypopharyngeal cancer.

The dietician should be involved starting at the moment of diagnosis to assess, monitor, and improve (if necessary) the patient's nutritional status.

Radiotherapy and Chemoradiation

Nutrition and fluid intake deserve close attention during and after treatment.

Nutritional Requirements During Radiotherapy and Chemoradiation

During radiotherapy and chemoradiation, patients should receive 130-150% of the basal metabolism in energy and 1.0-1.5 g protein per kg body weight per day (body mass index [BMI] 18.5-27).

Oral Feeding

Providing an individualised dietary therapy prepared by a specialised dietician is preferred over having other care providers oversee nutritional management and/or providing standard supplementation with liquid diets.

Gastrostomy Tube

When oral feeding no longer provides adequate nutrition and fluid, temporary or permanent tube feeding is indicated to limit weight loss and dehydration.

For patients who undergo chemoradiation, a gastronomy tube should be placed prior to treatment, give the high risk of long-term tube feeding during the radiation and rehabilitation periods.

If, prior to treatment, long-term tube feeding is expected to be necessary, preventive gastrostomy placement should be considered.

The decision to discontinue tube feeding or remove the gastronomy tube should be made in consultation with the dietician. The gastrostomy tube should only be removed after a period of adequate oral nutritional intake has been documented.

Surgery

The energy and protein content of perioperative tube feeding should be tailored to the individual needs of the patient. The need for tube feeding and changes in body weight should be evaluated regularly.

Immunonutrition

Based on the available evidence, immunonutrition does not have a role during the perioperative phase in patients with hypopharyngeal cancer.

Resuming Oral Feeding After Surgery

Patients should receive postoperative tube feeding, which guarantees adequate nutritional intake. Oral feeding can resume after the seventh postoperative day, provided that wound healing is uncomplicated, and can be increased gradually to achieve sufficient nutrition and normal consistency.

Postoperative Nutritional Problems

If swallowing or passage functions are disrupted, or if the senses of smell or taste lead to reduced intake of nutrition and fluids, the dietician should continue the dietary therapy until the situation stabilises. If necessary, the patient should be referred to a speech therapist (see "Swallowing rehabilitation" in the original guideline document).

Rehabilitation Period

If treatment-related eating disorders interfere with adherence to guidelines on proper nutrition, the goal should be to achieve adequate nutrition using nutrient-enriched products as needed.

Nutrition in the Palliative Phase

In patients with hypopharyngeal cancer and limited life expectancy, dietary measures should focus on patient well-being (i.e. quality of life is more important than long-term nutritional effects).

Eicosapentaenoic Acid [EPA]-Enriched Products for Tumour-Induced Cachexia

There is insufficient evidence at this time to recommend EPA-enriched products for patients with progressive weight loss due to tumour-induced cachexia.

Psychosocial Care

Patients with hypopharyngeal cancer are preferably seen not only by medical specialists but also by an oncology nurse and a social worker with expertise in the psychosocial issues of patients with head and neck cancer.

Contact with fellow patients should be offered, particularly for patients undergoing laryngectomy.

Patients with psychosocial issues should be referred to a psychologist, psychiatric nurse, or psychiatrist; these professionals can provide additional psychological diagnosis and help. These care providers should have experience in head and neck cancer. This type of support should also be offered during the first year of follow-up after treatment.

Palliative Care

Palliative Chemotherapy for Recurrent or Metastatic Squamous Cell Carcinoma of the Hypopharynx

Palliative chemotherapy should be considered for patients with recurrent or metastatic hypopharyngeal cancer if they have a WHO performance status of 0-2 and measurable disease, or if they have evaluable symptoms due to tumour growth, or if such symptoms are expected in the near future. Treatment within a clinical trial is preferred. Outside of a clinical trial, methotrexate is the treatment of choice; selected patients may receive combination chemotherapy (cisplatin + 5-fluorouracil).

Palliative Radiotherapy for Recurrent or Advanced Squamous Cell Carcinoma of the Hypopharynx

Palliative radiotherapy can be considered for patients with locoregional recurrence or advanced hypopharyngeal cancer who have disease-related symptoms or if such symptoms are expected in the near future. Fractionation can be individualised, depending on the patient's condition and life expectancy.

Palliative Surgery

Palliative surgery for patients with primary or recurrent hypopharyngeal cancer that cannot be treated curatively is limited to procedures that focus on the debulking of obstructive tumours using laser or diathermia.

Pain Management

The working group is of the opinion that first-line treatment for pain in patients with hypopharyngeal cancer should be given according to the WHO pain ladder

(see Appendix 13 in the original guideline document). Pain therapy can be more effective if patients receive information about the mechanism of pain and the optimal use of medication.

CLINICAL ALGORITHM(S)

An algorithm "World Health Organization (WHO) Pain Ladder" is provided in Appendix 13 of the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is reported in the conclusion section of each chapter in the original guideline document (see "Rating Scheme for the Strength of the Evidence" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate diagnosis and management of hypopharyngeal cancer
- Optimal approach to organ-sparing therapy

POTENTIAL HARMS

- Poor nutritional status negatively influences the course of disease and treatment outcomes. Complications, such as delayed wound healing and mucositis, persist longer and are more intense, and immunological defences are impaired.
- Chyle leakage after cervical lymph node dissection
- Hypothyroidism
- Toxicity and complications of radiotherapy and chemoradiation
- Serious functional impairment
- Psychosocial consequences

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Guidelines are not legal requirements, but rather scientifically founded and widely accepted views and recommendations to which healthcare providers would have to adhere to provide quality care. Given that guidelines are based on 'average' patients, healthcare providers can deviate from the recommendations in the guideline as necessary in individual cases. Deviation from the guideline may in fact be necessary in some cases. When there is deviation from the guideline, however, it must be rationalised, documented and, when necessary, discussed with the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation was considered throughout the various phases of development of the draft guideline. The guideline will be distributed to the board of directors of all hospitals, relevant scientific organisations, and Comprehensive Cancer Centres (Integrale Kankercentra). A summary of the guideline will also be published in the Dutch Journal of Medicine (Nederlands Tijdschrift voor Geneeskunde), and attention will be given to the guideline in various specialty journals. In addition, the guideline will be reproduced on www.nwhht.nl, www.oncoline.nl, and the Kwaliteitsinstituut voor de Gezondheidszorg (CBO) website. To stimulate implementation and evaluation of the guideline, the working group will subsequently create an implementation plan and a list of indicators, with which implementation can be measured. Indicators give healthcare providers the opportunity to assess whether they are providing the desired level of care. They can also be used to identify areas for improvement.

The guideline will be tested by end-users in various regions and scientific societies, and on-site inspections will be arranged.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Dutch Head and Neck Oncology Cooperative Group. Hypopharyngeal cancer. Amsterdam, The Netherlands: Association of Comprehensive Cancer Centres; 2007 Jan 9. 209 p. [904 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

Association of Comprehensive Cancer Centres - Disease Specific Society

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The guideline will be updated annually by a multidisciplinary committee created in 2006 based on scientific developments. The Dutch Head and Neck Oncology Cooperative Group, as the primary party responsible for the current guideline, will furnish the chairperson for this multidisciplinary committee. The committee has the responsibility of making interim inquiries by professional societies to establish the need for revision(s) of the current guideline. For important developments, it can be decided in agreement with CBO and VIKC to create interim electronic amendments and distribute them through the various professional societies. If necessary, a new study group will be created to revise the guideline or parts of it. The committee will install a new multidisciplinary study group for a complete revision of the guideline by no later than 2011.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Association of Comprehensive Cancer Centres Web site.

Print copies: Available from the Association of Comprehensive Cancer Centres PO Box 19001, 3501 DA Utrecht, The Netherlands.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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